

WHAT IS CLAIMED IS:

- 1 1. A luminal prosthesis comprising:
2 a scaffold which is implantable within a body lumen; and
3 means on the scaffold for releasing a substance, wherein the substance is
4 released over a predetermined time pattern comprising an initial phase wherein a substance
5 delivery rate is below a threshold level and a subsequent phase wherein the substance
6 delivery rate is above a threshold level.
- 1 2. A luminal prosthesis as in claim 1, wherein the scaffold is a stent or
2 graft.
- 1 3. A luminal prosthesis as in claim 1, wherein the scaffold is implantable
2 in a blood vessel.
- 1 4. A luminal prosthesis as in claim 1, wherein the substance comprises at
2 least one agent selected from the group consisting of immunosuppressant agent, anti-
3 inflammatory agent, anti-proliferative agent, anti-migratory agent, anti-fibrotic agent, anti-
4 thrombotic agent, anti-platelet agent, and IIb/IIIa agent.
- 1 5. A luminal prosthesis as in claim 4, wherein the agent is at least one
2 immunosuppressant agent selected from the group consisting of mycophenolic acid,
3 rapamycin, cyclosporine A, cycloheximide, cyclophosphamide, mizoribine,
4 methylprednisolone, azathioprine, ribovirin, FK506, tiazofurin, methotrexate, zafurin, and
5 mycophenolate mofetil.
- 1 6. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a matrix formed over at least a portion of the scaffold.
- 1 7. A luminal prosthesis as in claim 6, wherein the matrix is composed of
2 a material which undergoes degradation in a vascular environment.
- 1 8. A luminal prosthesis as in claim 7, wherein the matrix degrades by
2 surface degradation.
- 1 9. A luminal prosthesis as in claim 7, wherein the matrix degrades by
2 bulk degradation.

1 10. A luminal prosthesis as in claim 7, wherein the matrix is a copolymer
2 of poly-l-lactic acid and poly-e-caprolactone.

1 11. A luminal prosthesis as in claim 6, wherein the matrix is composed of
2 a nondegradable material.

1 12. A luminal prosthesis as in claim 11, wherein the nondegradable matrix
2 comprises cellulose acetate butyrate.

1 13. A luminal prosthesis as in claim 6, wherein the substance is disposed
2 within the matrix in a pattern that provides the desired release rates.

1 14. A luminal prosthesis as in claim 6, wherein the substance is on or
2 within the scaffold adjacent the matrix in a pattern that provides the desired release rates.

1 15. A luminal prosthesis as in claim 6, wherein the matrix comprises
2 multiple layers, each layer containing a different, same, or no substance.

1 16. A luminal prosthesis as in claim 6, further comprising a rate limiting
2 barrier coupled to the matrix.

1 17. A luminal prosthesis as in claim 6, further comprising a rate limiting
2 barrier formed over the matrix.

1 18. A luminal prosthesis as in claim 16 or 17, wherein the substance is
2 released by diffusion through the barrier.

1 19. A luminal prosthesis as in claim 6, further comprising a biocompatible
2 layer coupled to the matrix.

1 20. A luminal prosthesis as in claim 1; wherein the means for releasing the
2 substance comprises a rate limiting barrier formed over at least a portion of the scaffold.

1 21. A luminal prosthesis as in claim 20, wherein the rate limiting barrier
2 has a sufficient thickness so that release of the substance from the barrier begins substantially
3 after a preselected time period.

1 22. A luminal prosthesis as in claim 20, wherein the barrier has a thickness
2 in a range from 0.01 micron to 100 microns.

1 23. A luminal prosthesis as in claim 20, wherein the barrier is composed of
2 at least one material selected from the group consisting of silicone, polytetrafluoroethylene,
3 parylast, polyurethane, and paralene.

1 24. A luminal prosthesis as in claim 20, wherein the barrier comprises
2 multiple layers, each layer containing a different, same, or no substance.

1 25. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and a
3 cover over the reservoir, wherein the cover is at least partially degradable over a preselected
4 time period so that release of the substance from the reservoir begins substantially after the
5 preselected time period.

1 26. A luminal prosthesis as in claim 25, wherein the cover is a polymer
2 matrix.

1 27. A luminal prosthesis as in claim 25, further comprising a rate limiting
2 barrier formed between the reservoir and the cover.

1 28. A luminal prosthesis as in claim 25, further comprising a rate limiting
2 barrier coupled to the cover.

1 29. A luminal prosthesis as in claim 27 or 28, wherein the substance is
2 released by diffusion through the barrier.

1 30. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and a
3 cover over the reservoir.

1 31. A luminal prosthesis as in claim 30, wherein the cover having a
2 sufficient thickness so that release of the substance from the reservoir begins substantially
3 after a preselected time period.

1 32. A luminal prosthesis as in claim 30, wherein the cover is a
2 nondegradable matrix.

1 33. A luminal prosthesis as in claim 30, wherein the cover is a rate limiting
2 barrier.

1 34. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and an
3 external energy source for directing energy at the prosthesis after implantation to effect
4 release of the substance.

1 35. A luminal prosthesis as in claim 34, further comprising a matrix over
2 the reservoir.

1 36. A luminal prosthesis as in claim 34, further comprising a rate limiting
2 barrier over the reservoir.

1 37. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a matrix formed over at least a portion of the scaffold, wherein the
3 substance is disposed adjacent or within the matrix, and an external energy source for
4 directing energy at the prosthesis after implantation to effect release of the substance.

1 38. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a rate limiting barrier formed over at least a portion of the scaffold,
3 wherein the substance is disposed adjacent or within the barrier, and an external energy
4 source for directing energy at the prosthesis after implantation to effect release of the
5 substance.

1 39. A luminal prosthesis as in any of claims 34, 37, or 38, wherein the
2 energy source is at least one of ultrasound, magnetic resonance imaging, magnetic field, radio
3 frequency, temperature change, electromagnetic, x-ray, radiation, heat, gamma, or
4 microwave.

1 40. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to the substance or the scaffold and a

3 magnetic source for directing a magnetic field at the prosthesis after implantation to effect
4 release of the substance.

1 41. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to a matrix formed over the scaffold and a
3 magnetic source for directing a magnetic field at the prosthesis after implantation to effect
4 release of the substance.

1 42. A luminal prosthesis as in claim 41, wherein the substance is disposed
2 adjacent or within the matrix.

1 43. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises magnetic particles coupled to a rate limiting barrier formed over the
3 scaffold and a magnetic source for directing a magnetic field at the prosthesis after
4 implantation to effect release of the substance.

1 44. A luminal prosthesis as in claim 43, wherein the substance is disposed
2 adjacent or within the barrier.

1 45. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a change in a pH to effect release of the substance.

1 46. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises a reservoir on or within the scaffold containing the substance and
3 vibrational or heating energy directed at the prosthesis after implantation to effect release of
4 the substance.

1 47. A luminal prosthesis as in claim 1, wherein the means for releasing the
2 substance comprises at least a matrix or rate limiting barrier formed over the scaffold
3 containing the substance and vibrational or heating energy directed at the prosthesis after
4 implantation to effect release of the substance.

1 48. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is less than 12 weeks.

1 49. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 1 hour to 8 weeks.

1 50. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 12 hours to 2 weeks.

1 51. A luminal prosthesis as in claim 1, wherein the initial phase of
2 substance delivery is within a time period of 1 day to 1 week.

1 52. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 4 hours to 24 weeks.

1 53. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 1 day to 12 weeks.

1 54. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 2 days to 8 weeks.

1 55. A luminal prosthesis as in claim 1, wherein the subsequent phase of
2 substance delivery is within a time period of 3 days to 50 days.

1 56. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the initial phase is between 0 µg/day to 50 µg/day.

1 57. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the initial phase is between 5 µg/day to 30 µg/day.

1 58. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the subsequent phase is between 5 µg/day to 200 µg/day.

1 59. A luminal prosthesis as in claim 1, wherein the substance delivery rate
2 at the subsequent phase is between 10 µg/day to 100 µg/day.

1 60. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the initial phase is within a range from 0 µg/mg of tissue to
3 100 µg/mg of tissue.

1 61. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the initial phase is within a range from 0 µg/mg of tissue to
3 10 µg/mg of tissue.

1 62. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the subsequent phase is within a range from 1 picogram/mg
3 of tissue to 100 µg/mg of tissue.

1 63. A luminal prosthesis as in claim 1, wherein a mammalian tissue
2 concentration of the substance at the subsequent phase is within a range from 1 nanogram/mg
3 of tissue to 10 µg/mg of tissue.

1 64. An improved method for delivering a pharmacological agent to an
2 artery, said method being of the type where a prosthesis is implanted within the artery and the
3 prosthesis releases the pharmacological agent, wherein the improvement comprises
4 implanting a prosthesis that is programmed to begin substantial release of the
5 pharmacological agent beginning after growth of at least one layer of cells over a part of the
6 prosthesis.

1 65. A method as in claim 64, wherein the cells comprise inflammatory,
2 smooth muscle, or endothelial cells.

1 66. A method as in claim 64, wherein the pharmacological agent
2 comprises at least one agent selected from the consisting of immunosuppressant agent, anti-
3 inflammatory agent, anti-proliferative agent, anti-migratory agent, anti-fibrotic agent, anti-
4 thrombotic agent, anti-platelet agent, and IIb/IIIa agent.

1 67. A method for luminal substance delivery, said method comprising:
2 providing a luminal prosthesis incorporating or coupled to the substance,
3 wherein the prosthesis contains a matrix which undergoes degradation in a vascular
4 environment; and
5 implanting the prosthesis in a body lumen so that at least a portion of the
6 matrix degrades over a predetermined time period and substantial substance release begins
7 after the matrix substantially begins to degrade.

1 68. A method as in claim 67, wherein the substance is incorporated in a
2 reservoir in or on a scaffold and the reservoir is covered by the matrix so that substantial
3 substance release begins after the matrix has degraded sufficiently to uncover the reservoir.

1 69. A method as in claim 67, wherein the substance is contained in the
2 matrix and the matrix coats a scaffold, wherein an outer layer of the matrix is substantially
3 free from the substance so that substance release will not substantially begin until the outer
4 layer has degraded.

1 70. A method as in claim 67, wherein the substance is contained within or
2 on a scaffold coated by the matrix.

1 71. A method as in claim 67, wherein the prosthesis is coated with the
2 matrix by spraying, dipping, deposition, or painting.

1 72. A method as in claim 67, wherein the prosthesis incorporates the
2 substance by coating, spraying, dipping, deposition, or painting the substance on the
3 prosthesis.

1 73. A method as in claim 67, wherein the matrix is a polymer.

1 74. A method as in claim 67, wherein the matrix comprises multiple
2 layers, each layer containing a different, same, or no substance.

1 75. A method as in claim 67, wherein the prosthesis contains a rate
2 limiting barrier adjacent the matrix coating.

1 76. A method as in claim 67, wherein the matrix degrades by surface
2 degradation.

1 77. A method as in claim 67, wherein the matrix degrades by bulk
2 degradation.

1 78. A method for luminal substance delivery, said method comprising:
2 providing a luminal prosthesis incorporating and/or coupled to the substance,
3 wherein the prosthesis contains a rate limiting barrier; and
4 implanting the prosthesis in a body lumen so that substantial substance release
5 from the barrier begins after a preselected time period.

1 79. A method as in claim 78, wherein the barrier has a sufficient thickness
2 to allow diffusion of the substance through the barrier.

1 80. A method for luminal substance delivery, said method comprising:
2 providing a luminal prosthesis incorporating or coupled to the substance,
3 wherein the prosthesis contains a nondegradable matrix; and
4 implanting the prosthesis in a body lumen so that substantial substance release
5 from the nondegradable matrix begins after a preselected time period.

1 81. A method as in claim 80, wherein the nondegradable matrix has a
2 sufficient thickness to allow diffusion of the substance through the nondegradable matrix.

1 82. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 4 hours to 24 weeks in a vascular environment.

1 83. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 1 day to 12 weeks in a vascular environment.

1 84. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 2 days to 8 weeks in a vascular environment.

1 85. A method as in any of claims 67-81, wherein substantial release of the
2 substance begins within a time period of 3 days to 50 days in a vascular environment.

1 86. A method for luminal substance delivery, said method comprising:
2 implanting a luminal prosthesis in a lumen of a patient, wherein the prosthesis
3 incorporates and/or couples a substance to be released into the lumen or a luminal wall; and
4 directing energy at the prosthesis to effect release of the substance from the
5 prosthesis.

1 87. A method as in claim 86, wherein the prosthesis incorporates the
2 substance by coating, spraying, dipping, deposition, or painting the substance on the
3 prosthesis.

1 88. A method as in claim 86, wherein the substance is incorporated in a
2 reservoir in or on a scaffold containing the substance.

1 89. A method as in claim 86, wherein the substance is incorporated in a
2 matrix and the matrix coats a scaffold.

1 90. A method as in claim 86, wherein the energy is at least one of
2 ultrasound, magnetic resonance imaging, magnetic field, radio frequency, temperature
3 change, electromagnetic, x-ray, radiation, heat, gamma, or microwave.

1 91. A method for releasing a substance from an implanted device, said
2 method comprising:

3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to the substance; and
5 directing a magnetic field at the device to effect release of the substance from
6 the device.

1 92. A method for releasing a substance from an implanted device, said
2 method comprising:

3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to a matrix formed over the device; and
5 directing a magnetic field at the device to effect release of the particles from
6 the device.

1 93. A method for releasing a substance from an implanted device, said
2 method comprising:

3 implanting a device in a patient, wherein the device incorporates magnetic
4 particles coupled to a rate limiting barrier formed over the device; and
5 directing a magnetic field at the device to effect release of the particles from
6 the device.

1 94. A kit comprising:

2 a luminal prosthesis; and
3 instructions on how to implant the prosthesis for luminal substance delivery
4 according to any one of claims 64-93.

1 95. A luminal prosthesis comprising:

2 a scaffold which is implantable within a body lumen; and
3 means on the scaffold for releasing two substances, wherein the two
4 substances are released over two predetermined time patterns comprising an initial phase

5 wherein a substance delivery rate is below a threshold level and a subsequent phase wherein
6 the substance delivery rate is above a threshold level.

1 96. A prosthesis as in claim 95, wherein the means for releasing the two
2 substances comprises a matrix having multiple layers formed over at least a portion of the
3 scaffold.

1 97. A prosthesis as in claim 95, wherein the means for releasing the two
2 substances comprises a rate limiting barrier having multiple layers formed over at least a
3 portion of the scaffold.

1 98. A prosthesis as in claim 95, wherein the two substances are released at
2 different time patterns.

1 99. A prosthesis as in claim 95, wherein a second substance is released
2 after a threshold level of a first substance is reached.

1 100. A prosthesis as in claim 95, wherein the two substances are released
2 simultaneously.

1 101. A prosthesis as in claim 95, wherein the two substances are
2 sequentially released.